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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SKOWRONEK, KARLHEINZ R	
ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/823,509	RAJH ET AL.	
	Examiner	Art Unit	
	KARLHEINZ R. SKOWRONEK	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 28-41* is/are pending in the application.

4a) Of the above claim(s) *1 and 37-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-36 and 41* is/are rejected.

7)☒ Claim(s) *36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1 and 28-41 are pending.

Claims 2-27 are cancelled.

Claims 1 and 37-40 are withdrawn as being directed to a non-elected invention, the election having been made in the replies of 10 September 2007, 18 May 2007, and 28 November 2006.

Claim 41 is new.

Claims 28-36 and 41 have been examined.

Claims 28-36 and 41 are rejected.

Claim 36 is objected to.

Priority

This application claims priority to Application No. 10/755045 filed on 9 January 2004 as a continuation of Application No. 09/606,429 filed on 28 June 2000.

Claim Objections

Claim 36 is objected to because of the following informalities: Clam 36 recites TIO_2 which is a typographical error for TiO_2 as no atomic element with the abbreviation of upper case (t) and upper case (i) exists. The claim will be treated as reciting TiO_2. Appropriate correction is required.

Claim Rejections - 35 USC § 103

Response to Arguments

Applicant's arguments, see Remarks p. 5-7, filed 21 April 2008, with respect to the rejection(s) of claim(s) 28 and 34-35 as unpatentable over Empedocles in view of Chan in view of Wamer and in further view of Knowland under 35 USC 103(a) have been fully considered. The rejection has been withdrawn in view of the amendment of the claims. However, upon further consideration, a new ground(s) of rejection is made below over Empedocles et al., in view Ogawa, in view of Falaras, in view of Bergstrom et al., in view of Chan et al., and in view of Wamer et al.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The following rejection is modified as necessitated by amendment of the claims.

Claims 28-36 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Empedocles et al. (US PGPUB 20030099940), in view Ogawa (Annu. Rep. Prog. Chem., Sect. C: Phys. Chem., Vol. 94, p. 209 - 225, 1998), in view of Falaras (Solar Energy Materials and Solar Cells, Vol. 53, p. 163-175,1998), in view of Bergstrom et al. (Bioorganic & Medicinal Chemistry Letters, Vol. 6, No. 18, pp. 2211-2214, 1996), in view of Chan et al. (Science, Vol. 281, p2016-2018, 1998), and Wamer et al. (Free Radical Biology and Medicine, Vol. 23, No. 6, p, 851-858, 1997).

The claim is directed to a method of manipulating biological material in vivo by introducing a semiconductor-complexed biological moiety into a living organism and causing a structural change in the biological material. In an embodiment, the biological material is nucleotides. In an embodiment, charges are created by radiation.

Empedocles et al. shows a method of attaching a semiconductor, also referred to as a quantum dot [0061], to a biological moiety [0111]. Empedocles et al. defines the term affinity moiety as a biological moiety [0045-0046]. Empedocles et al. shows the affinity moiety is attached to the semiconductor nanocrystal [0119]. Empedocles shows

that TiO_2 is used [114]. Empedocles shows an embodiment in which the semiconductor is attached to affinity molecules that are polynucleotides [0174].

Empedocles et al. does not show the covalent attachment of a semiconductor to a biological moiety through a charge transfer intermediary, bioconjugated semiconductor particle is introduced into a living organism or that by irradiating the semiconductor particle bioconjugate the biological material is changed.

Ogawa shows that the surface modification of semiconductor colloids can extend the response of the colloid toward low-energy excitations. Ogawa shows surface modification can be achieved by attaching dyes on the colloid surface (p. 224). Ogawa shows that in order to extend the photo-response of large band gap semiconductor materials, such as TiO_2, the charge from the excited state of the attached dye is injected into the conduction band of the semiconductor (p. 224). Ogawa shows that the photo-excited dye transfers an electron to the semiconductor. Ogawa shows that the efficiency of charge separation depends on the relative magnitude of the electron transfer rate constant to the rate of back electron transfer and non-radiative decay of the adsorbed dyes (p. 224).

Falaras shows TiO_2 can form covalent linkages with the dye or metal-complex, Ru-bipyridine (scheme 1). In table 2, Falaras shows that TiO_2 complexes have photo-activation wavelengths between 450 and 570 nm, which is about 2ev to about 2.8ev. Falaras shows that the most efficient sensitizers at the time achieved a maximum efficiency on the order of 90% in a broad band of the visible spectrum, reading on radiation that has an energy of 1.6 eV and on the range of 1.6 eV-3.2 eV (p. 171).

Bergstrom et al. shows that nucleic acids can be labeled with metal-bipyridine complexes. Bergstrom et al. shows that chemical nucleases formed by linking redox metal to nucleotides leads to an improvement in the specificity and efficiency of nucleic acid cleavage (p. 2211). Bergstrom shows activation of the redox metal using peroxide as a source of hydroxyl radical (p. 2213).

Wamer et al. shows that by irradiating TiO_2 with 400nm light, structural changes in DNA can be obtained. Wamer et al. shows that nucleic acid is photo-oxidized in the presence of light-activated TiO_2 (p. 855, col. 1-2). Wamer et al. shows an embodiment in which 400 nm light is used (p. 852, col. 2). Wamer et al. shows an embodiment in which charges are created by radiation (p. 851, col. 1). Wamer et al. shows an embodiment in which the radiation has energy greater than 1.6 eV, (p. 851, col. 1). Wamer et al. shows a plurality of charges is generated using light to the induced structural changes in nucleic acid as oxidative damage (p. 856, col. 2). Wamer et al. suggests that TiO_2 should be adsorbed to DNA, that is, a bioconjugate formed between TiO_2 and DNA (p. 857, col. 1). Wamer et al. suggests that TiO2 may be a useful photodynamic therapy of cancer (p. 851, col. 2). Wamer et al. shows that irradiated TiO_2 is a catalyst for a variety of redox reactions that include decarboxylation of carboxylic acids and hydrogen production from carbohydrates and water. Wamer et al. shows that TiO_2 provides the advantage of possessing antibacterial activity when irradiated (p. 851, col. 2).

Chan et al. shows that quantum dots can be introduced into living organisms (p. 201, col. 3). Chan et al. shows bioconjugated quantum dot migrates to a target

biological material within a cell (figure 4). Chan shows that quantum dots have an advantage over conventional fluorophores of an improved photo-stability (p. 2018, col. 2).

It would have been obvious to one of ordinary skill in the art to modify the TiO_2 of Empedocles by binding it to bipyridine dyes of Falaras et al. because Ogawa et al. shows that binding of TiO_2 with dyes sensitizes the TiO_2 to advantageously extend the photo-response of TiO_2 lower energy wavelengths. It would have further obvious to modify the dye of Falaras by binding to nucleic acids as in Bergstrom et al. because Bergstrom et al. shows that binding of bipyridine dyes to nucleic acids has the advantage of efficiently and specifically directing the oxidative cleavage of nucleic acid. It would have further obvious to one of ordinary skill in the art to introduce the TiO_2-bipyridine nucleic acids of Empedocles et al., in view of Ogawa, in view of Falaras et al. and in view of Bergstrom et al. into a living organism because Chan et al. show the successful introduction of nanocrystal labeled biological molecules into cells have the advantage of increased photo-stability. It would have been further obvious to modify the method of attaching a semiconductor particle to a biological molecule of Empedocles et al., in view of Ogawa, in view of Falaras and in view of Bergstrom et al. in view of Chan et al. with the method of inducing structural changes in biological material by generating a plurality of charges of Wamer et al. because Wamer et al. shows that the semiconductor particle, TiO_2 has photo-dependent oxidative activity that is capable of damaging biological material such that the particle has antibacterial activity. It would have been further obvious to one of ordinary skill in the art to modify the method of

attaching a semiconductor particle to a biological molecule of Empedocles et al., in view of Ogawa, in view of Falaras and in view of Bergstrom et al. with the introduction into cells to produce structural alterations in the biological material of Chan et al. and Wamer et al. because all the claimed elements were known in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention.

Response to Arguments

Applicant's arguments filed 21 April 2008 and 30 October 2008 have been fully considered but they are not persuasive. Applicant argues that Empedocles et al. does not qualify as prior art because the filing date of Empedocles et al. is predated by applicants effective filing date of 28 June 2000. The argument is not persuasive. The date relied upon is the filing date of the provisional application of Empedocles et al. which has the date of 16 February 2000. See 35 USC 119(e) and 35 USC 102(e). Applicant argues that Chan et al. fails to teach *in vivo* applications of semiconductor nanocrystals citing p. 2017, col. 3 as support. This is not persuasive because p. 2017, col. 3 of Chan et al. states “we demonstrated that quantum dots (QD) were biocompatible in vitro and **with living cells**.” Emphasis added by examiner. The fact that Chan distinguishes “in vitro” from “living cells” at least suggests that Chan encompasses in vivo applications of quantum dots. Chan et al. further shows that quantum dots were used in vivo on p. 2018, col. 1 by stating "when transferrin was

present, receptor mediated endocytosis occurred, and the luminescent QDs were transported into the cell." A cell is a "living organism," as recited in the claims. Applicant argues the size of the quantum dot in Chan. The argument is not persuasive because Chan et al. demonstrate the introduction of biological molecules modified with semiconductor nanocrystals or QDs. Thus the semiconductor nanocrystals of Chan meet the limitations of the claims. Furthermore, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., semiconductor nanocrystal size) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicants argue Wamer et al. teaches away from the instant method because Wamer et al. states that TiO_2 does not absorb visible light. This is not persuasive because Ogawa shows that the photo-response of TiO_2 can be shifted to lower energy wavelengths through the use of dye sensitizers or charge transfer intermediaries. In addition, Falaras et al. shows the shift of TiO_2-Ru-bipyridine covalent complex to the range of 450-570 nm, which is visible. Applicant argues Wamer et al. uses 320nm light. Applicant misrepresents the teaching of Wamer et al. While Wamer et al. does teach that TiO_2 does not absorb visible light, Wamer also teaches the use of light in the range of 320-400 nm, or 3.8 eV-3.1eV as sufficient for exhibiting the antibacterial activity of TiO_2 (p. 851, col. 2).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLHEINZ R. SKOWRONEK whose telephone number is (571)272-9047. The examiner can normally be reached on 8:00am-5:00pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/K. R. S./
Examiner, Art Unit 1631

22 January 2009

/Marjorie Moran/
Supervisory Patent Examiner, Art Unit 1631